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Clinical features of giant hybrid ameloblastoma of the mandible: A case report with long-term observation of natural growth before treatment

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ABSTRACT

Hybrid ameloblastoma comprising desmoplastic and solid type ameloblastoma with classic follicular or plexiform pattern is a known unusual variant. Ameloblastoma, including the hybrid type, is a slow growing tumor, and there is very little information regarding growth of such tumors when left untreated. We present here the clinical features of a giant hybrid ameloblastoma of the mandible together with extended radiographic observation before the patient consented to surgery. A 62-year-old Japanese man was referred in 2002 with a chief complaint of a left-sided mandibular swelling. Panoramic X-ray showed a multilocular radiolucent lesion extending from the left mandibular angle to the ascending ramus, including an impacted wisdom tooth with root resorption. Biopsy specimen examination revealed myxofibrous tissue with some odontogenic epithelial nests. The clinical diagnosis was odontogenic myxoma or myxofibroma of the left side of the mandible. At that time, the patient declined surgical treatment. The tumor gradually increased in size over 7 years of follow-up, and he finally consented to undergo surgical treatment when the tumor began approaching the skull base. Tumorectomy including hemimandibulectomy and plate reconstruction of the mandible were performed in 2009. Histopathology revealed follicular and desmoplastic ameloblastoma with myxomatous change and was diagnosed as hybrid ameloblastoma. No recurrence was seen at the 24-month follow-up examination, and mandibular reconstruction using bone regeneration and oral rehabilitation with a dental implant were performed. Further clinicopathological analysis of coexisting desmoplastic ameloblastoma and non-desmoplastic ameloblastoma is needed to understand the significance and biological behavior of this hybrid variant.

1. Introduction

Ameloblastoma is a benign odontogenic tumor, accounting for 1% of all cysts and tumors of the jaw and 11% of all odontogenic tumors. It has a tendency for aggressive invasion of the jaw, a high rate of recurrence, and rare malignant transformation with lymph node metastasis [1]. Ameloblastoma is localized to the maxilla in 20% of cases and to the mandible in the remaining 80%. Over 57% of

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ameloblastomas in the mandible are located in the molar region or ascending ramus [2]. According to the 2005 World Health Organization classification of odontogenic tumors, ameloblastoma can be further classified as solid/multicystic, extraosseous/peripheral, desmoplastic, and unicystic types. Several histopathological patterns of ameloblastoma have been reported, including follicular, plexiform, acanthomatous, keratinizing, granular cell, basal cell, desmoplastic, and spindle cell. The treatment depends on the subtypes of ameloblastoma. Solid/multicystic and desmoplastic types are treated by excision with an adequate margin of uninvolved tissues and extraosseous/peripheral type is treated by conservative excision. In unicystic type, enucleation could be carried out for luminal variant and further surgical intervention in mural variant must be considered depending on the depth of epithelium invasion into the cyst wall [3]. In 1987, Waldron and El-Mofty first reported an unusual variant described as a "hybrid" lesion, consisting of both desmoplastic ameloblastoma and solid ameloblastoma with a classic follicular or plexiform pattern [4].

Ameloblastoma is considered a slow-growing tumor and is generally treated with either conservative management or radical

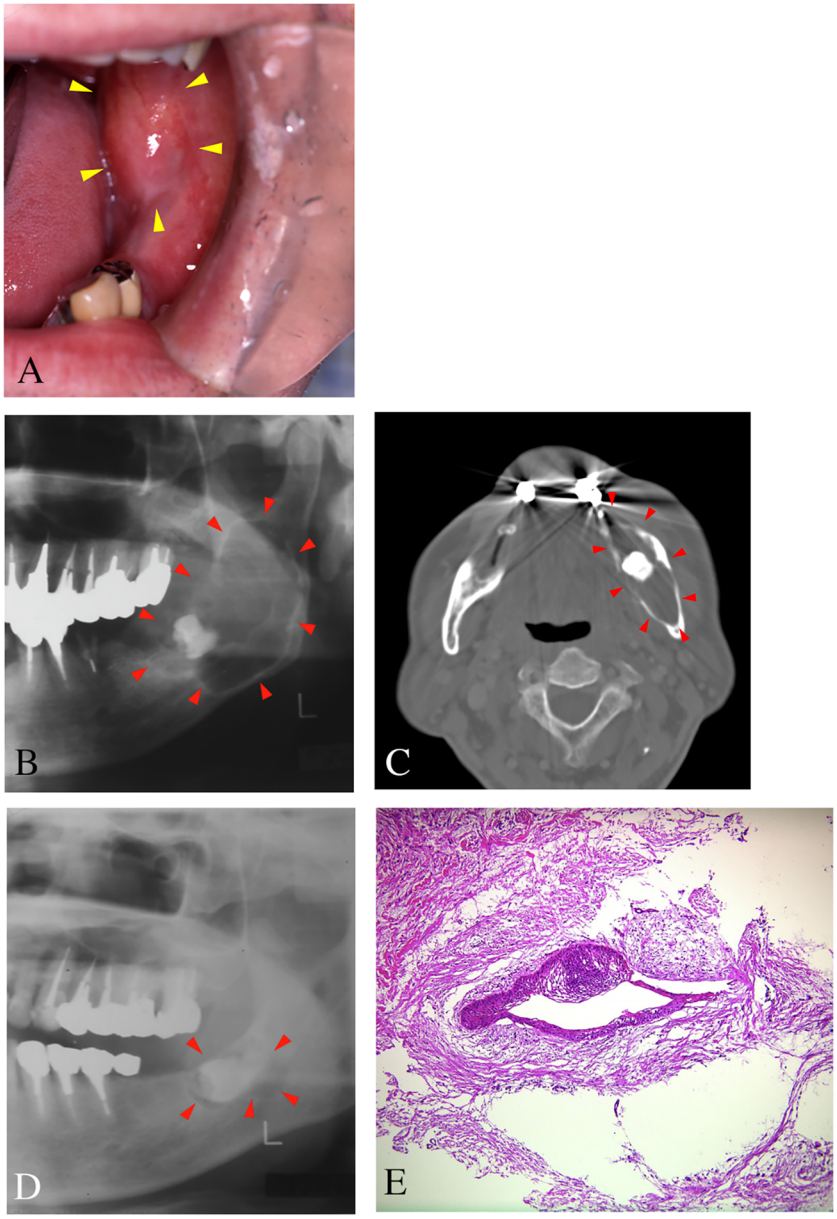

Fig. 1. (A) Intraoral photograph shows swelling from the left retromolar to ascending ramus region. (B) Panoramic X-ray shows a multilocular radiolucent lesion including an impacted wisdom tooth with root resorption. (C) Axial computed tomography shows an expanded low-density area in the left-side mandible with cortical bone resorption including an impacted wisdom tooth. (D) Panoramic X-ray in 1996 shows a radiolucent area is apparent under the lower left wisdom tooth (image courtesy of the patient's dental practitioner). (E) Histopathological features of the biopsy specimen (hematoxylin and eosin stain; original magnification, ×10) include myxofibrous tissue with odontogenic epithelium.

surgery at the time of first presentation. Therefore, few studies offer any information about the growth of these tumors if left untreated [5–7]. This clinical case report presents a rare case of a giant hybrid ameloblastoma of the mandible that was observed radiographically during an extended period of growth before the patient finally consented to surgery.

2. Case report

A 62-year-old Japanese man was referred to the Department of Oral and Maxillofacial Surgery of Shimane University Hospital in June 2002 with a chief complaint of swelling on the left side of the mandible. He had a past medical history of hepatitis type C and idiopathic thrombocytopenic purpura and was being followed up with treatment for both conditions. On initial examination, the lower aspect of the face appeared symmetrical, but a bony swelling was found intraorally extending from the left retromolar region to the ascending ramus (Fig. 1A). There was no pain or paresthesia in the left mental region. Panoramic X-ray showed a multilocular radiolucent lesion, including an impacted left lower wisdom tooth accompanied by root resorption, in the ascending ramus region. The radiolucent area is apparent under the lower left wisdom tooth in the panoramic X-ray in 1996, which was provided by the patient's dental practitioner (Fig. 1B–D). The clinical diagnosis was odontogenic tumor, possibly keratocystic odontogenic tumor, ameloblastoma, or myxoma, of the left side of the mandible. Examination of a biopsy specimen taken from the intraosseous lesion revealed myxofibrous tissue with some odontogenic epithelium (Fig. 1E), and the pathological diagnosis was odontogenic myxoma or myxofibroma. We explained the clinical diagnosis and the need for tumorectomy and segmental mandibulectomy to the patient but he declined surgical treatment therefore, only follow-up examinations were undertaken. The tumor gradually expanded, with further asymmetry of the lower face due to increased swelling (Fig. 2). The patient continued to refuse surgical treatment during the next 7 years of follow-up but finally consented when the tumor began to approach the skull base (Fig. 2C). Tumorectomy including hemimandibulectomy and reconstruction of the mandible using a titanium plate were performed in December 2009 under general anesthesia (Fig. 3). The excised specimen was $135 \times 90 \times 80$ mm and weighed 437 g.

Histopathologically, the tumor consisted mainly of odontogenic epithelium with a follicular pattern (indicative of follicular

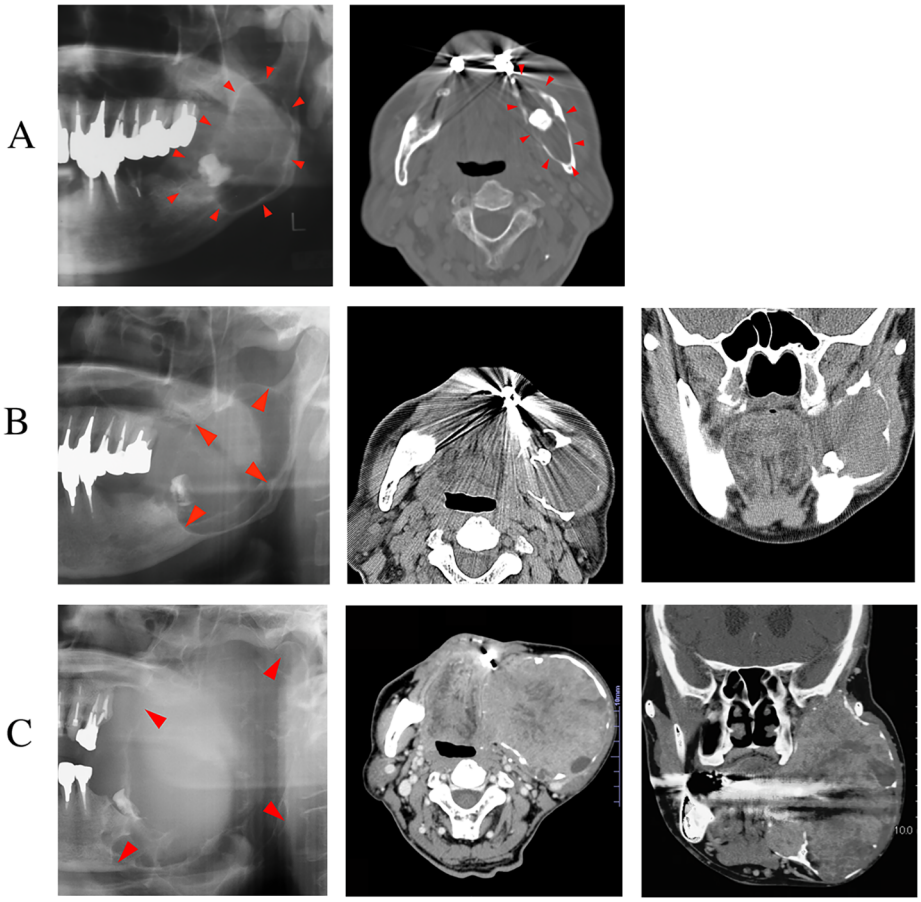

Fig. 2. Panoramic X-rays and computed tomography show gradual expansion of the lesion in the retromolar to ascending ramus region. (A) In 2002, a multilocular radiolucent area has expanded in the left ascending ramus, with root resorption. (B) In 2004 (left image) and 2005 (middle and right image), further expansion of the multilocular lesion in the retromolar to ascending ramus region is apparent. (C) In 2009, the lesion has expanded past the ascending ramus and is approaching the skull base.

ameloblastoma) and massive fibrosis with a few areas of odontogenic epithelial nests and myxomatous change (indicative of desmoplastic ameloblastoma), with well-circumscribed fibrous and bony tissue. The pathological diagnosis was hybrid ameloblastoma. The specimen also had components of follicular, desmoplastic, plexiform and acanthomatous patterns (Fig. 4A–D). In this case, the diagnostic difference between the biopsy specimen and the resected specimen was due to the biopsy specimen being obtained from the component of the ameloblastoma that had myxomatous change (Fig. 4E). The postoperative course was uneventful, and no recurrence was seen at a 24-month follow-up examination. According to the patient's opinion of minimum reconstruction surgery, mandibular reconstruction to the left mandibular angle region using distraction osteogenesis and oral rehabilitation using a dental implant was planned. The mandibular defect was reconstructed with a 55.5-mm bone distraction and 4 dental implants were placed in the native and reconstructed bone. A denture supported by the 4 implants was fabricated. Although the concavity of the left side of the face still remained, esthetic and masticatory disturbance resolved postoperatively (Fig. 5). No recurrence has been seen for 9 years since the initial surgical treatment.

3. Discussion

Waldron and El-Mofty described hybrid ameloblastoma as having a predilection for the posterior region of the mandible [4], and other investigators have reported the anterior and posterior regions of the mandible as frequently affected sites [8,9]. Hybrid lesions are rare, with a relative frequency of 5/116 ameloblastoma cases (4.3%) in the report by Waldron and El-Mofty [4] and 2/58 ameloblastoma cases (3.4%) in a study performed by Higuchi et al. [8]. Furthermore, Takata et al. reported only one hybrid case among 92 ameloblastoma cases (1.1%) [9]. In hybrid lesions, areas of solid ameloblastoma usually display plexiform and follicular patterns [4,8,9]. Rarely, these solid areas show basal cell, granular cell, or squamous metaplasia or acanthomatous patterns [9,10].

In our case, the tumor was located in the mandibular molar region extending to the ramus region and displayed follicular, plexiform, acanthomatous, and desmoplastic components, similar to those described in previous reports. It is not clear whether hybrid lesions are due to areas of desmoplastic ameloblastoma transforming into solid ameloblastoma, desmoplastic change occurring in solid ameloblastoma, or multiple tumors coalescing into one lesion [11]. However, Melrose et al. state that the "hybrid" tumor designation serves no real purpose and, if taken literally, could overstate the significance of the findings of desmoplastic ameloblastoma in combination with islets of solid ameloblastoma [12]. Furthermore, Fulco et al. reported the identification of focal areas of desmoplastic ameloblastoma in 22.4% of solid lesions [10], supporting the opinion of Melrose et al. [12].

Although cases of giant ameloblastoma have been reported in developing countries, they are rare in developed countries today because the tumors are usually treated early and do not become large. However, even in developed countries, giant ameloblastoma can occur when a patient delays treatment because of fear of undergoing surgery. In this case, the absence of pain, the minimal disturbance of mouth opening, speech, and mastication, and minimal facial distortion—which are all directly related to quality of life—may have contributed to the patient's delayed consent to surgical treatment.

In an estimation of the monthly growth rate of ameloblastoma, Odukoya and Effiom reported that solid/multicystic ameloblastoma has the fastest growth rate and the peripheral subtype the slowest (tumor volume increase of 0.81 vs 0.17 cm^3/month, respectively), and that desmoplastic ameloblastoma may be less biologically aggressive compared with the solid/multicystic type (tumor diameter increase of 0.36 vs 0.71 cm/month, respectively) because desmoplasia acts as a tumor-limiting barrier [5,6]. In contrast, Chae et al. [7] calculated ameloblastoma growth rates using the formula for specific growth rate (SGR) described by Mehrara et al., which more accurately reflects the natural exponential growth of the tumor [13]. However, similar to Odukoya and Effiom [5,6], a meta-analysis found the highest estimated growth rate is associated with a solid/multicystic pattern and the lowest rate with peripheral ameloblastomas, with a mean SGR of ameloblastoma of 87.84% per year [7]. In the present case, SGR was 62.54% per year, which is relatively low compared with the 16 cases reported by Chae et al.; however, their analysis used symptom duration to represent disease duration in the SGR formula. Odontogenic tumors of the maxilla or mandible are generally asymptomatic at onset and are often found accidently on radiographic examination in many cases. Therefore, the SGR calculated in our case is likely more accurate than that in

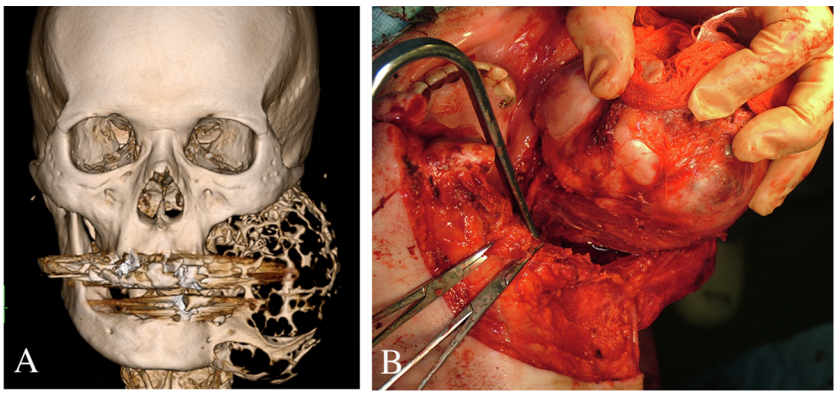

Fig. 3. (A) Three-dimensional computed tomography shows the expanded lesion approaching the skull base with destruction of the mandible. (B) Intraoperative photograph shows the tumorectomy using lower cheek flap approach.

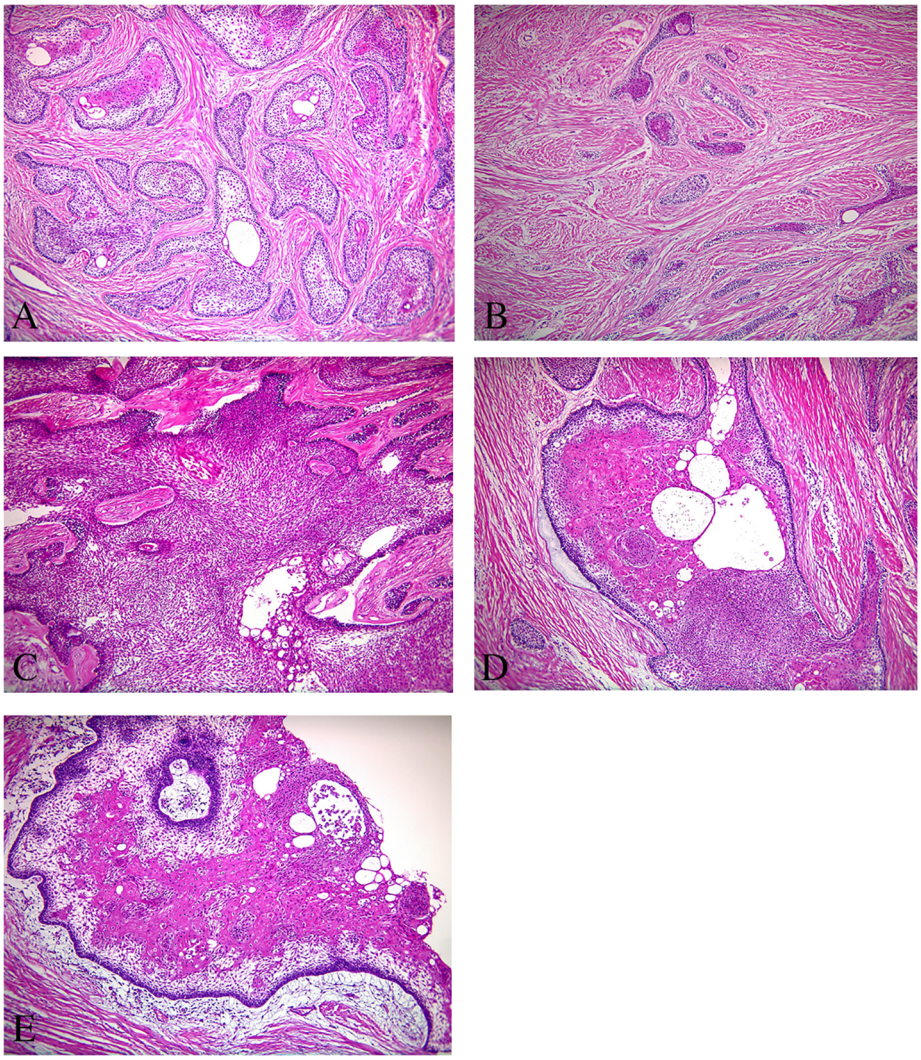

Fig. 4. Histopathological features of the resected specimen (hematoxylin and eosin stain; original magnification, ×10) include hybrid ameloblastoma with (A) follicular, (B) desmoplastic, (C) plexiform, and (D) acanthomatous patterns and (E) a component of myxomatous change.

the study by Chae et al., because a panoramic X-ray taken 6 years before the initial presentation in our hospital (Fig. 1D) revealed onset of the ameloblastoma in the absence of symptoms. Impacted tooth and its subsequent resorption with radiolucent area like our case would present the initial finding of the onset of odontogenic lesion. Natural history of ameloblastoma is various due to the subtypes and coexisting of the histopathological patterns like hybrid ameloblastoma. Amount of desmoplastic component in the whole tumor may influence to the natural history of the hybrid ameloblastoma because the desmoplastic ameloblastoma may be less aggressive due to the desmoplasia acting as a tumor-limiting barrier [6].

Various radiographical appearances of hybrid ameloblastomas have been summarized by Effiom et al. [14]. Hybrid lesions generally exhibit mixed radiolucent and radiopaque patterns with irregular borders, similar to those commonly observed in desmoplastic lesions (with osteoplasia), fibro-osseous lesions, and malignant tumors, while a few cases exhibit a multilocular radiolucent pattern similar to that of conventional ameloblastoma. In the present case, the multilocular radiolucent lesion with irregular border gradually increased in size over 11 years, with absorption of the impacted third molar.

The most appropriate treatment for hybrid ameloblastoma is resection with an adequate margin of uninvolved tissue, similar to the treatment for desmoplastic ameloblastoma and conventional solid ameloblastoma [3]. Desmoplastic ameloblastomas have ill-defined margins and may have a tendency to recur at least as often as conventional ameloblastomas [4,9]. Recurrence is a main complication of inadequately treated lesions and is influenced by factors such as anatomical location and the clinicopathological variant of the lesion. Excluding unicystic ameloblastoma (which has a less aggressive nature), surgical resection with a bony margin of 1–2 cm and immediate reconstruction is currently indicated [15]. In our case, the surgical margin was insufficient because the lesion was enormous and located close to the skull base; therefore, a staged reconstruction after follow-up examination was performed rather than immediate reconstruction using a free flap such as a fibular flap.

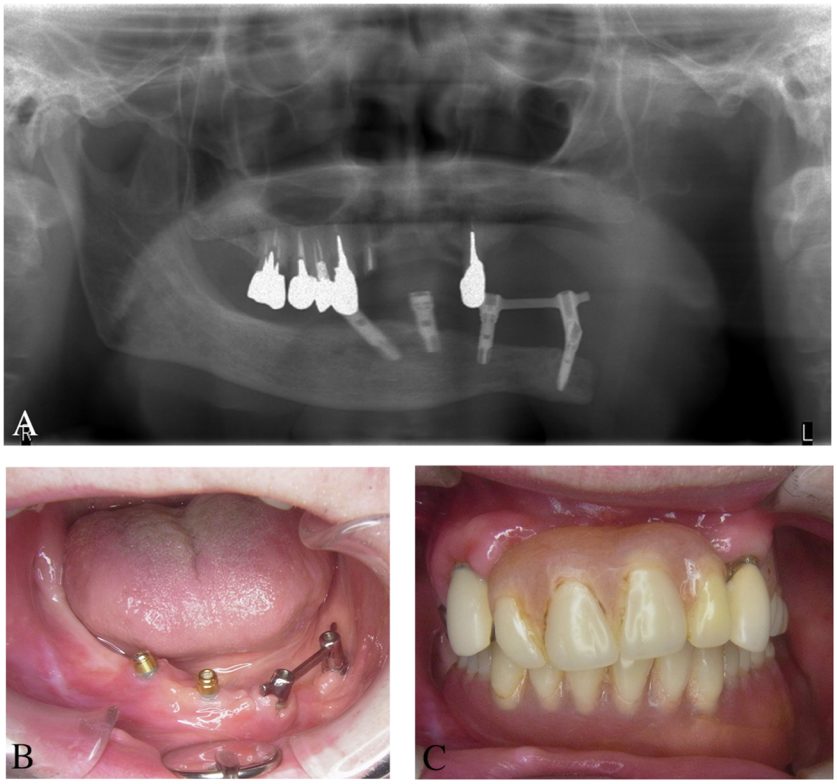

Fig. 5. (A) Panoramic X-ray shows 4 dental implants placed in the native and reconstructed mandible. (B) Intraoral photograph shows 2 locator abutments and bar attachment connected to the implants. (C) Intraoral photograph shows the lower denture in place, supported by the implants.

Hybrid ameloblastoma is a rare variant, and the significance and biological behavior of coexisting desmoplastic ameloblastoma and non-desmoplastic ameloblastoma are unknown. Further clinicopathological analysis of this variant is needed.

Conflicts of interest

The authors report no conflicts of interest.

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